REMARKS

Independent claims 1 and 140 have been amended to further highlight their patentability over the prior art of record. Dependent claims 3, 4, 6, 141 and 143 have also been amended, and claims 5 and 142 canceled. Dependent claims 2 and 7-41 remain unchanged.

Applicants also present arguments below in further support of the patentability of all claims in view of the rejections set forth in the pending Office Action.

Claims 1-41 And 140-143 Stand Rejected Under 35 U.S.C. §103(a)

Claims 1-41 and 140-143 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 6,468,506 to *Rŏssling et al.* in view of U.S. Patent 5,885,216 to *Evans, III et al.* and further in view of U.S. Patent 6,231,513 to *Daum et al.* or International Pub. WO96/40282 to *Quay et al.*

In summary, the Office Action apparently reports that each of the claims essentially recites a process whose result would produce a product that would be the same as that produced by a combination of the cited prior art, and hence that such claims are unpatentable under §103(a) given the product-by-process proscriptions cited in In re Thorpe, 777 F.2d 695, 698,227 USPQ 964,966 (Fed Cir. 1985). See MPEP 2113.

Applicants respectfully believe that such a conclusion is incorrect even before consideration of the amendments herein. Nevertheless, Applicants have amended the claims to more definitively set forth the subject matter they wish to claim. In doing so, Applicants believe that they have overcome the suggestion that any process inherent in the pending claims produces a product that is the same as or obvious from whatever type of product that could be produced from a combination of the prior art.

Independent claim 1, for example, is directed to a system for creating a bubble medium for administration into a patient. Among other limitations, this claim recites a *controller* through which "an operator [can] monitor or change at least one operating parameter of the system and thus at least

one property of the medium real time inclusive of the bubbles therein." Consequently, the "medium is generated for real time administration into the patient so as to optimize according to the demands of the operator a medical procedure being performed on the patient."

The prior art cited above, however, neither individually nor collectively teach or even suggest such a system. More specifically, the systems and apparatuses of the prior art are in no way directed to a system whose controller is capable of real time control of the properties of the bubbles in a medium that is being prepared for real time administration into a patient.

As explained in Applicants previous response dated 5 February 2008 and incorporated herein by reference, the *Rössling et al.* patent only teaches the making of dried microparticles to which water is to be added later for purpose of re-hydrating to create a bubble-based contrast medium. It discloses a method of making dried spherically-shaped microparticles in which a gas (e.g., air) is enclosed. (col. 2, lines 1-2; col. 9, line 65) The last step of the method involves removing the dried microparticles from column 19, as shown in Figure 1. (col. 5, lines 28-33; col. 10, lines 32-36) The dried micro-particulate product is then destined for packaging and shipment for later use at sites where ultrasound imaging procedures can be performed. Once delivered to such a site, the dried microparticles can then be suspended in a pharmaceutically acceptable suspension medium (e.g., water) to create the contrast agent. (col. 3, lines 60-67) Unlike Applicants' claims, the *Rössling et al.* patent thus does not disclose a system whose controller is capable of real time control of the properties of the bubbles in a medium that is being prepared for real time administration into a patient.

Similarly, the *Evans, III et al.* patent, either alone or in combination with the *Rössling et al.* patent, also does not teach the system recited in claim 1. Instead, it discloses a process/system that permits contrast of varying concentration to be injected into a patient. The bottom line is that the

Evans, III et al. patent teaches only the mixing of contrast to the desired concentration and delivery of same into the patient. (col. 5, lines 60-61; col. 6, lines 38-40)

While the *Evans, III et al.* patent discloses a system for diluting contrast to a desired concentration level and administering same into a patient, it teaches nothing about real time control/change of the properties of the bubbles in a medium for administration into a patient and into whom it can be immediately administered/injected.

Furthermore, the size of the dried microparticles created by the method of *Rössling et al.* is entirely dependent on the size, shape and type of nozzle used in their manufacture. (column 3, lines 49-51) Therefore, if the teaching of *Rössling et al.* could be combined with those of *Evans, III et al.*, it would certainly not yield a contrast dilution system in which the properties of the bubbles could be controlled real time and then, for example, administered immediately into a patient. This is because, for example, any such change in microparticle size would require a different nozzle to be installed in the apparatus of *Rössling et al.*, which Figure 1 suggests is an arduous and time-consuming task -- a manual task that is contrary to the real-time control of bubble generation of Applicants' claims. In this regard, *Evans, III et al.* in fact teach away from what the Applicants have claimed in the present application.

The *Daum et al.* and *Quay et al.* references are likewise inapposite to buttress the pending 35 U.S.C. §103(a) rejection.

The *Daum et al.* patent discloses devices that are inserted into a blood vessel wherein they are used to form microbubbles in the blood for use in ultrasonic imaging procedures. One such device is a needle 20 in whose pointed distal end 21 is housed a beveled porous matrix 23. When the needle 20 is inserted into a vessel, gas passes through the lumen 24 and flows through the porous matrix 23 resulting in the formation of microbubbles in the blood. (col. 3, lines 57-63) Another such device features a needle 101 at the proximal end 103 of which is affixed a piezoelectric ultrasound transmitter 102. In operation, the distal end of needle 101 is inserted into a vessel. Gas from a source thereof then flows

via connector 105 through the hollow shaft of needle 101 and into the vessel. While that is happening, ultrasonic waves formed by activation of transmitter 102 causes vibrations that break the flow of the gas into microbubbles within the blood stream. (col. 4, lines 10-23)

The *Quay et al.* publication discloses a method/apparatus for forming a "microbubble-containing solution" and then administering that solution to an animal. (p. 22,lines 4-8; p. 23, lines 1-5 & 13-15) The solution is formed only in bulk volume (Id. & p. 8, lines 6-25), i.e., all at one time, and it is formed using an activation method, which *Quay et al.* expressly define as only through the use of "a hypobaric force on [the] solution." (p. 5, line 36 - p. 6, line 3) In other words, the apparatus of *Quay et al.* creates bubble-based media only in bulk volume and only in response to the lowering of pressure in the container in which the solution is stored. Consequently, unlike the system recited in the pending claims, the apparatus of *Quay et al.* is not capable of creating, and hence altering the characteristics of, the bubbles on the fly, as the demands of the medical procedure change. The real-time control of Applicants' claimed system over the bubble generator recited in the claims makes this possible.

The *Daum et al.* patent pertains only to creation of bubbles directly within a blood vessel by means of gas injected via a needle. The *Quay et al.* publication pertains only to bulk formation of a bubble contrast medium, which is then injected into the blood stream. Neither reference discloses a system whose a controller permits an operator to change/control real time the properties of the bubbles in the medium, which is, for example, then promptly administered into a patient.

Finally, even if the teachings of *Rõssling et al.* could be combined with those of *Evans, III et al.*, at best they would yield a contrast dilution system to which the dried microparticles of *Rõssling et al.* would somehow be added. This mixture might result in a diluted bubble contrast medium but one in which the size and other characteristics of the bubbles are all the same. The system of independent claims 1 and 140 and their respective dependents, however, permit production of a medium in which the properties of the bubbles and the overall medium can be varied real time. Claim 6 recites some of

the properties that can be changed on the fly, e.g., the composition of the medium, the composition of the bubbles in the medium, the concentration of the bubbles in the medium, the size of the bubbles in the medium, the rate of flow of the medium, the volume of the medium administered, the timing of the administration of the medium, the sequencing of the administration of the medium, the pressure of the medium and the temperature of the medium can all be controlled real time according to the demands of the operator during a medical procedure (e.g., an imaging procedure).

Applicants believe that they have overcome the suggestion that any process inherent in their claims produces a product that is the same as or obvious from whatever type of product that could be produced from a combination of the prior art. In Applicants' claims, the real time control of the properties of the bubbles and the medium overall preclude such a conclusion. Applicants respectfully submit that the foregoing arguments successfully refute the notion that such claims are unpatentable under §103(a) in view of the product-by-process proscriptions cited in In re Thorpe, 777 F.2d 695, 698,227 USPQ 964,966 (Fed Cir. 1985). See MPEP 2113.

For the above reasons, Applicants respectfully submit that combined teachings of *Rŏssling et al.*, *Evans, III et al.* and *Daum et al.* or *Quay et al.* do not render obvious the subject matter recited in independent claims 1 and 140 and their dependents 2-4 & 6-41 and 141& 143, respectively. In view of the foregoing amendments and arguments, Applicants believe that the §103(a) rejections have been overcome.

CONCLUSION

Before entry of this *Amendment And Response*, the present application had forty-five (45) claims pending, two (2) of which independent. Upon entry of this *Amendment And Response*, the application will contain forty three (43) claims, two (2) of which independent. Earlier in prosecution, ninety eight (98) claims were withdrawn with traverse due to an restriction requirement.

Given the foregoing amendments and arguments, Applicants respectfully request withdrawal of the rejections set forth in the Office Action dated 20 August 2008. Applicants believe the application is ready to be allowed. If the Examiner has any questions regarding this *Amendment and Response*, he is invited to call the undersigned at the telephone number listed below.

Respectfully submitted,

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I hereby certify that this correspondence is being electronically filed with the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on 19 February 2009.

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